CORRELATION BETWEEN MITRAL ANNULAR SYSTOLIC VELOCITY AND LEFT ATRIAL APPENDAGE FUNCTION IN MITRAL STENOSIS

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CERTIFICATE

This is to certify that the dissertation titled "**CORRELATION BETWEEN MITRAL ANNULAR SYSTOLIC VELOCITY AND LEFT ATRIAL APPENDAGE FUNCTION IN MITRAL STENOSIS"** is the bonafide original work of Dr**. M. S. SELVAKUMARAN**, in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2014.The period of post-graduate study and training was from August 2011 to July 2014.

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DECLARATION

I, **Dr. M. S. SELVAKUMARAN**, solemnly declare that this dissertation entitled, "**CORRELATION BETWEEN MITRAL ANNULAR SYSTOLIC VELOCITY AND LEFT ATRIAL APPENDAGE FUNCTION IN MITRAL STENOSIS**" is a bonafide work done by me at the department of Cardiology, Madras Medical College and Government General Hospital during the period 2011 – 2014 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor M. S. Ravi M.D.D.M. This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **D.M. Degree (Branch-II) in Cardiology**.

Place: **SIGNATURE OF THE CANDIDATE**

Date:

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CONTENTS

INTRODUCTION

The appendage of the left atrium is bulbar structure which is long with a narrow junction at its meeting point with left atrium. In many diseases the left atrial appendage is clinically important because of the propensity for the development of thrombus. Being a dynamic structure, the stasis of blood is prevented, but when its function is impaired, stasis will increase. This may lead to the development of spontaneous echo contrast and thrombus formation. Moreover an inactive left atrial appendage is an independent predictor of thrombo embolism. Hence the decision for anticoagulant therapy can be made on the basis of the presence of inactive left atrial appendage.

In patients with rheumatic mitral stenosis, left atrial appendage velocities are reduced. Also in mitral stenosis, the annular velocities calculated by Doppler tissue imaging are reduced. The lateral mitral annulus and the left atrial appendage has a close functional and anatomic relation and hence the velocities obtained from the annulus by Doppler tissue imaging may reflect left atrial appendage functions.

The prevalence of rheumatic heart disease is high in South Asian countries, particularly in India. Isolated mitral stenosis occurs in 25% of all rheumatic heart disease cases. Mitral stenosis and mitral regurgitation occur in 40% of the cases. Almost two thirds of patients with mitral stenosis are females. The thrombi originating from the left atrial appendage are believed to be the source of embolism in patients with rheumatic mitral stenosis, especially when mitral stenosis is associated with atrial fibrillation.

Echocardiography is used to detect thrombi in the left atrium and its appendage. Transthoracic echocardiography is 50% sensitive in detecting left atrial and left atrial appendage thrombi. Transesophageal echocardiography (TOE) is superior to transthoracic echocardiography and has high sensitivity and specificity for the detection of left atrial and left atrial appendage thrombi. The individual valve lesion severity can be assessed by echocardiography in patients with rheumatic heart disease and can be matched with left atrial dimensions and hence used for risk stratification from thromboembolism.

Effective blood flow in the appendage cavity prevents thrombus

formation, but disease states like atrial fibrillation and rheumatic heart disease cause left atrial appendage dysfunction and becomes a risk factor for thrombus formation. Recent attention has been focused on left atrial appendage function by transesophageal echocardiography to assess the risk of thrombus formation.

Spontaneous echo contrast in left atrium is a common finding in patients with rheumatic mitral valve disease. Left atrial spontaneous echo contrast is an independent predictor for systemic embolization and is documented better by transesophageal echocardiography. In this scenario it is prudent to investigate whether there is a relation between mitral annular velocities obtained by Doppler tissue imaging and left atrial appendage function and to find out if the velocities obtained from the annulus can indicate the presence of inactive left atrial appendage in patients with mitral stenosis.

AIMS AND OBJECTIVES

1. To determine the relation between systolic mitral annular velocity and left atrial appendage function by Doppler tissue imaging.
2. To investigate if the systolic mitral annular velocity can indicate the presence of inactive left atrial appendage in mitral stenosis.
3. To assess echocardiographic parameters particularly left atrial dimensions, mitral valve area, presence of left atrial thrombus and spontaneous echo contrast by trans-thoracic echocardiogram.
4. Trans-esophageal echocardiographic assessment of thrombus, spontaneous echo contrast and emptying velocity of appendage of left atrium.
5. To determine if there is any correlation between E wave or A wave velocities and left atrial appendage emptying velocity.
6. To risk stratify thromboembolism in those patients based on Doppler echocardiographic parameters.
7. The ultimate aim of the study is to prevent thromboembolism in all mitral stenosis patients especially who are in sinus rhythm.

REVIEW OF LITERATURE

Valvular heart disease remains a major burden in India. Due to lack of diagnostic facilities in many areas especially in rural areas, it is mandatory to be familiar with assessment of valvular heart disease at the bedside by physical examination. With escalating health care costs, cost effectiveness of care (diagnostic and therapeutic) is important. The attending physician has the responsibility of using limited economic resources of the patient in an appropriate way.

In India rheumatic heart disease remains the commonest cause of valvular heart disease. Less common causes are Degenerative, Congenital and Infective Endocarditis. Rare causes include drug induced, trauma, carcinoid syndrome, connective tissue disorders, iatrogenic etc. Previously considered as an insignificant structure in cardiac anatomy, the appendage of left atrium is now considered a structure with important pathological associations.[1]

The risk of cerebrovascular accident is increase approximately four to

five fold in non-rheumatic atrial fibrillation and fifteen fold in patients with rheumatic mitral stenosis and atrial fibrillation. In rheumatic mitral valve disease there is a predilection for thrombus formation in left atrial appendage, especially in atrial fibrillation and it is also is present in sinus rhythm. In non-valvular atrial fibrillation also clot formation occurs in left atrial appendage. With the advent of transesophageal echocardiography now it is possible to assess in health and disease, the shape, flow patterns, size and content of left atrial appendage.

Atrial fibrillation is the causative factor for about 15% of cardio-embolic ischemic cerebro vascular accidents.[2] As a whole 90% of thrombus originates in the left atrial appendage in non-valvular atrial fibrillation. Around 60% of thrombus were seen in appendage of left atrium in rheumatic mitral valve disease. The thromboembolic phenomenon can be reduced with the use of anti-coagulants and some patients have contraindications for the initiation of such treatment. In those patients who have contraindications for OAC (Oral Anti-Coagulants) an alternative form of thromboembolism prophylaxis is warranted.

ANATOMY OF THE LEFT ATRIAL APPENDAGE

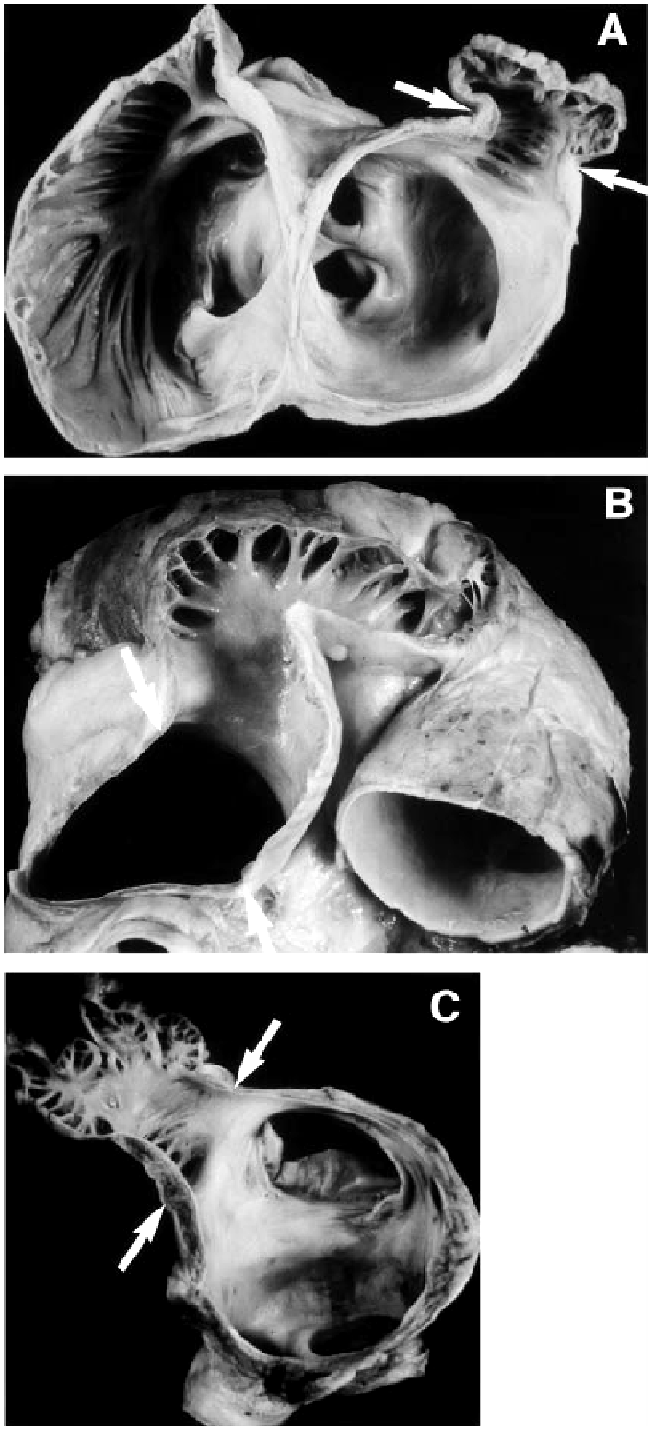
The left atrium develops in 3rd week of gestation.[3] The appendage of the left atrium is a remnant of embryonic left atrium. The main left atrium develops from the outgrowth of pulmonary veins. The left atrial appendage is much longer than its counterpart on the right side and has a much narrower connection with the atrium. The shape of the left atrial appendage resembles a finger or the wing of a bird. The left atrial appendage is a tubular and hooked structure. In contrast the right atrial appendage has a broad base and a triangular contour and resembles the ear of a dog. Both appendages have trabeculation and both appendages have pectinate muscles, which are nothing but muscles running parallel to each other, resembling a comb.

The right atrial appendage has prominent pectinate muscles whereas it is less prominent in the left atrial appendage. In some congenital heart diseases the pectinate muscles in appendages were used to identify the morphological left and right atrium. In autopsy studies, in patients with atrial fibrillation the atrial appendages were voluminous and broader when compared to patients in sinus rhythm. These findings correlate with transesophageal echocardiography findings in different imaging planes. [4]

These findings may be due to hemodynamics of atrial fibrillation or atrial fibrillation per se.

Figure showing various types of LAA

A) Single lobed B) Bilobed C) Multilobed



The myocytes in appendage of left atrium is similar to the myocyte of myocardium present in other sites. The left atrial appendage has a thicker epicardium when compared with the thickness over the ventricles. The left atrial appendage is an intra-pericardial structure. It is related superiorly to the pulmonary artery and to the free wall of the left ventricle inferiorly. The blood supply to the left atrium comes from the left atrial branch of left circumflex artery and from the right coronary arteries. They are innervated by both sympathetic and parasympathetic system.

PHYSIOLOGY

The contraction pattern of left atrial appendage is distinct. When compared to left atrium it shortens to a greater extent. Transesophageal echocardiography has been used for studying the blood flow within the left atrial appendage. It gives optimal views of appendage and its orifice.

The left atrial appendage flow patterns in those patients who are in sinus rhythm which was measured by Doppler imaging techniques were described as biphasic.[5] In addition to the biphasic flow pattern there were emptying and filling waves. This is called quadriphasic flow pattern. [6] This flow pattern was described in 50-70% of patients. This quadriphasic flow pattern is seen much more commonly in healthy volunteers. This flow

pattern may not be seen in patients undergoing transesophageal echocardiography for clinical indications.

There are 2 phases in the left atrial appendage flow, a forward flow phase and a backward flow phase. In the forward flow phase the blood moves out of the appendages. This phase occurs early in the diastole, after the start of the trans-atrial flow this is followed by a short phase of backward flow, in which blood moves into the appendage.

The causal relationship between early left atrial appendage emptying and the left ventricular relaxation is suggested by the first forward flow phase. This first forward flow phase is fixed to the beginning of early diastole. A further phase of forward flow is noted due to the contraction of the left atrial appendage coincides with atrial systole. This is followed by backward flow phase. This backward flow phase is presumably caused by the elasticity of the left atrial appendage. This cyclic forward flow and backward flow phase is constant and independent of heart rate.

The left atrial appendage being intrapericardial is relatively fixed and immobile. It is in close relation with pulmonary artery in superior aspect and

to the free wall of left ventricle inferiorly and medically. The intrapericardial space is being filled up during disease as the left ventricle dilates. This dilation of left ventricle during diastole compresses the inferomedial wall of left atrial appendage between the fixed pericardium and its free wall. This has been suggested to contribute to the emptying of the left atrial appendage.

During early diastole and intracavitary suction effect is created by ventricular filling. This intracavitary suction effect will have an influence on the filling and emptying of left atrium as well as the left atrial appendage. Hence the filling and emptying of left atrial appendage is influenced by changes in left ventricular function rather than appendage function. This finding will explain the atrial fibrillation related cerebrovascular accidents in patients with left ventricular dysfunction. [7] There was an inverse relationship between the filling and emptying of left atrial appendage and ventricular rate. These findings can be extrapolated for and optimal rate control in the prevention of thromboembolism in atrial fibrillation. [8]

There are theories regarding whether the left atrial appendage contracts actively or it functions passively. This is due to the relation of the left ventricular filling and left atrial appendage flow, the latter being

compressed by left ventricle during ventricular diastole and also the negative pressure created by ventricular filling empties the appendage.

The left atrial appendage has prominent muscle ridges. If these pectinate muscle ridges won't contract, they will go for atrophy. Hence the evidence favours active contraction of left atrial appendage. If the filling and emptying in the appendage is passive, this will not explain the quadriphasic flow pattern which was seen at low heart rates. Cardiac surgeons have also observed active contraction of left atrial appendage intraoperatively.

The distensibility of the left atrial appendage is much more that the proper left atrium. There will be an increase in dimensions as well as left atrial pressure when appendage is clamped during cardiac surgery. There is also an increase in pulmonary and trans-mitral diastolic flow velocities during clamping of the appendage.[9] By way of modulating left atrial pressure volume relations the left atrial appendage will increase hemodynamic function in states of pressure and volume overloaded left atrium, this is due to the increased distensibility of the left atrial appendage.

About 30% of all cardiac atrial natriuretic factor were present in atrial

appendages. The density of atrial natriuretic factor granules was high in the left atrial appendage. Amyloidosis has predilection for left atrial appendage. The major protein in atrial amyloidosis is atrial natriuretic factor.

The neural supply to atrial appendages is diverse. There will be an increase in urine flow and sodium excretion, when the atrial appendage is distended experimentally without increasing the pressures in the right or left atrium or aorta. This is due to the stretch sensitive receptors in the atrial appendage. When bases of both appendages were crushed this effect is lost.

The stretch receptors also cause an increase in the heart rate mediated by the sympathetic efferent pathway. Hence left atrial pressure is maintained by left atrial appendage via stretch sensitive receptors which when activated increase natriuresis, heart rate and diuresis. Also the distensibility of left atrial appendage and through atrial natriuretic factor secretion helps maintain the left atrial pressure. [10]

IMAGING OF THROMBUS IN LEFT ATRIAL APPENDAGE

Left atrial appendage lies between the left ventricle and pulmonary outlet region in a normal cardiac skiagram. Previously angiography has been used extensively for diagnosing thrombi in the left atrial appendage. [11]

Being an invasive procedure it is not done nowadays. Transthoracic echocardiography has limited diagnostic utility in the imaging of thrombus in left atrial appendage.

A highly accurate imaging was done through transesophageal echocardiography. This semi-invasive imaging technique is a valuable tool for diagnosing thrombus in the left atrial appendage. For diagnosing thrombi in left atrial appendage transesophageal echocardiography has 100% sensitivity and 99% specificity. The positive predictive value of transesophageal echocardiography for diagnosing left atrial appendage thrombus is 86% and a negative predictive value is 100 %.[12]

If the length of the time in atrial fibrillation is more than 48 hours, current guidelines recommend oral anticoagulation at least 3 weeks prior to and 4 weeks following direct current cardioversion.[13] A transesophageal echocardiogram can be performed while the patient is on intravenous heparin with a goal aPTT of 1.5 to 2.0 and if no identifiable thrombus is found, direct current cardioversion can safely be performed, followed by oral anti-coagulants with a goal INR of 2.0-3.0.[14]

In the assessment of cardioversion using transesophageal echocardiogram (ACUTE) study, transesophageal echocardiography screening of patients with atrial fibrillation prior to cardioversion was

compared to conventional approach based on 3 weeks of anti-coagulant therapy. Both groups were continued on warfarin for 4 weeks after the cardioversion. There was no difference noted in the embolic event rate or maintenance of sinus rhythm, TEE cardioversion minimized the duration of atrial fibrillation and increases the likelihood of success. [15]

The size, flow velocity and flow patterns of left atrial appendage are related to thrombus formation. An enlarged left atrial appendage is associated with thrombus formation and subsequent embolisation as evidenced by studies with transesophageal echocardiography. Around 60% of patients with enlarged left atrium on transesophageal echocardiography have and enlarged left atrial appendage. About 15% of the patients with a normal left atrium have an enlarged left atrial appendage.

A light grey haze which was swirling inside the great vessels and veins had cardiac chambers called spontaneous echo contrast (SEC) first described by Feigenbaum in 1975 is observed in conditions of low blood flow velocity such as rheumatic mitral stenosis, dilated left atrium, dyskinetic segments of left ventricle and mitral valve prosthesis. SEC represents intracardiac erythrocyte or platelet microaggregates. It may be a precursor for thrombus formation.

In patients with left atrial appendage thrombus, left atrial appendage size is larger both in patients with sinus rhythm and atrial fibrillation. In patients with chronic atrial fibrillation the appendage area is significantly larger in patients with thrombus when compared with patients who do not have thrombus. [16]

Velocity and Pattern of Flow in Left Atrial Appendage

The velocity of flow at the orifice of the appendage is determined by Doppler TOE. In patients in sinus rhythm and atrial fibrillation and absent or reduced left atrial appendage inflow and outflow velocities were associated with spontaneous echo contrast and formation of thrombus.

In patients with history of systemic embolization the left atrial appendage filling and emptying velocities are reduced. [17] Based on Doppler transesophageal echocardiography the pattern of flow in left atrial appendage is classified into three types :[5]

Type 1 – Sinus rhythm patients with regular pattern of filling and emptying.

Type 2 – Atrial Fibrillation patients with saw tooth pattern

Type 3 – Atrial Fibrillation patients with no waves identified.

The incidence of thrombus formation and spontaneous echo contrast is high in patients with type 3 flow pattern, when compared with type 1 and type 2. The flow patterns were related to the appearance of fibrillatory waves on the electrocardiogram. In coarse atrial fibrillation the left atrial appendage ejection fraction and emptying velocity were reduced and this was associated with a high incidence of thrombus and spontaneous echo contrast. Patients with fine atrial fibrillation have lesser incidence of thrombus and SEC.

There are two proposed causes for left atrial appendage dysfunction in patients with atrial fibrillation:

1. Myopathic process resulting in atrial Fibrillation

2. Atrial fibrillation resulting in myopathic process

In patient with atrial flutter, left atrial appendage flow pattern shows a regular pattern and high emptying velocities when compared to patients in atrial fibrillation. Hence atrial flutter will have low incidence of thromboembolism. [18]

The thromboembolic risk is determined by the size as well as the mobility of the thrombus. A thrombus that are pedunculated, mobile and more than 15 cm are at high risk for thromboembolism. Post cardioversion with drugs or with DC shock, some of the patients with atrial fibrillation will

have decreased mechanical function of left atrium for a variable period, following reverting to sinus rhythm. Studies on left atrial appendage function also show depressed mechanical function following cardioversion. [19]

The inflow and outflow velocities of the left atrial appendage are decreased following successful cardioversion of atrial fibrillation. Spontaneous echo contrast also develops after successful cardioversion. The depressed atrial function results in thrombus formation. The term stunning is used to denote depressed atrial mechanical function after cardioversion.

DC cardioversion per-se causes damage to the atrium and appendage with the resulting depressed function and stasis. This was challenged by the subsequent studies on patients, which showed that stunning also occur in pharmacological as well as spontaneous cardioversion.

Atrial mechanical dysfunction is not seen in patients who receive shock for ventricular tachycardia. The depressed atrial mechanical function following cardioversion is due to atrial and left atrial appendage myopathy caused by atrial fibrillation. The depression of function is also related to the chronicity of atrial fibrillation.

Patients in sinus rhythm, with underlying left ventricular dysfunction are also associated with left atrial thrombus formation. [20] About 15% of

patients with dilated cardiomyopathy, in sinus rhythm have thrombi in the left atrial appendage. A small proportion of patients with history of TIA, stroke, systemic embolism without significant carotid stenosis do have thrombi in left atrial appendage.

The continuous formation and dissolution of thrombi in left atrial appendage makes it a dynamic process. This has been correlated to raised serum concentrations of Fibrinopeptide A, that reflects thrombin mediated fibrin formation and D- dimer which is a fibrinogen degradation product. [21]

Patients who were treated with warfarin for 4 weeks, showed clot dissolution which was confirmed by transesophageal echocardiography. The disappearance of thrombi suggests that the clot formation and lysis is a dynamic process. The role of endothelium and platelets in left atrial appendage clot formation is not known.

Warfarin is used in the prophylaxis of stroke in atrial fibrillation. Because of its narrow therapeutic index and bleeding complications alternative treatment such as obliteration of left atrial appendage can be tried. The procedure is technically challenging and may result in unfavorable hemodynamic and hormonal effects which could have an impact on patients with left ventricular dysfunction and valvular heart disease. Left atrial appendage is the sole location of thrombi in only about 60% of patients with

mitral valvular disease. Hence left atrial appendage obliteration will not prevent all episodes of thromboembolism.

Echocardiographic Assessment of Left Atrial Appendage

The assessment of appendage function was described initially by Suetsugu et al and by Pollick and Taylor and has now become incorporated into the routine transesophageal examination.[23,24] The imaging of left atrial appendage has been done primarily in 2 basic biplane tranesophageal views, the horizontal and longitudinal views.[22]

1. The horizontal view is a short axis view at the base of the heart
2. The longitudinal view is a two chamber view of the left ventricle and atrium.

The appendage can be visualized in a continuum of intermediate planes by multi-plane Transesophageal echocardiography. Transpulmonary injection of contrast agents have been used to improve the Doppler recordings and echocardiographic images to visualize the appendage. Left atrial appendage is a posterior cardiac structure.

Transesophageal imaging can easily visualize left atrial appendage. By transthoracic echocardiography, left atrial appendage can be imaged by parasternal short axis view at the level of base of heart and also by apical

two chamber view. However transesophageal approach is necessary for adequate visualization of left atrial appendage especially in elderly population. Recently it has been suggested that Doppler imaging of appendage can be done through transthoracic approach.

A complete assessment of left atrial appendage includes 2D imaging of its size, morphology and contraction. A quantitative assessment of left atrial appendage function is done through pulse-Doppler imaging of left atrial appendage flow.[25] In addition the left atrial size, left ventricular systolic and diastolic function and the associated mitral valve disease should be assessed and correlated with the left atrial appendage function,

2D Evaluation of Left Atrial Appendage

Previously the appendage area and ejection fraction has been calculated. This is not relevant clinically because the appendage cross sectional area is inclined to have considerable inter-observer variability. This is due to the fact that appendage is a complex structure and hence the standard imaging is limited.

The assessment of left atrial appendage function by planimetry method is time consuming and it doesn't offer any advantage over gross estimation of left atrial appendage size and function. In contrast Doppler

imaging of left atrial appendage function can be performed easily. It is also reproducible and relevant clinically.

In an autopsy study about 80% of atrial appendage was multi lobed and 59% was bilobed. The appendage should be imaged precisely be a multi plane trans-esophageal echocardiogram.

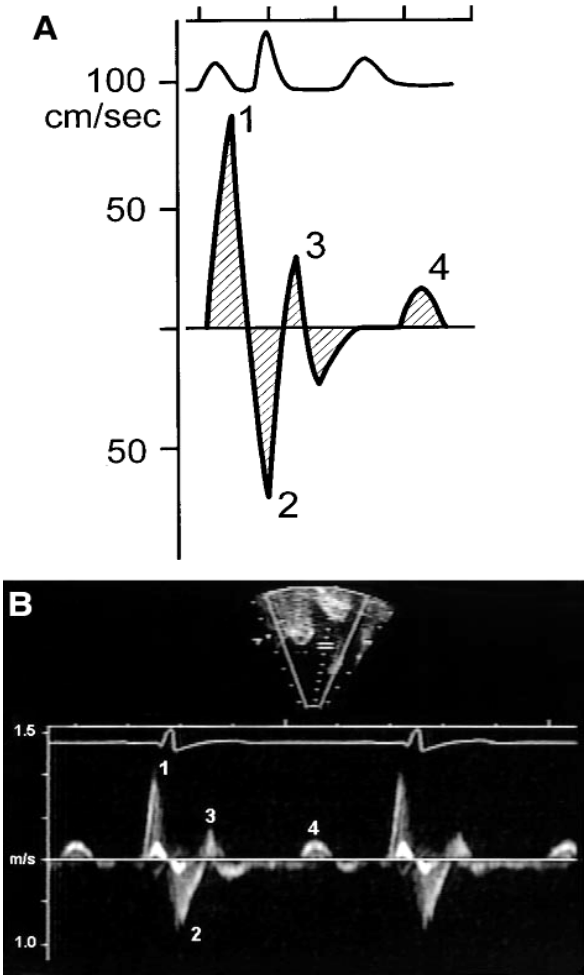
The presence of spontaneous echocardiographic contrast and its semi quantitative grading and also the presence of complex structure of left atrial appendage, trans-esophageal echocardiography will both over diagnose and under-diagnose the lesions.[26] There may be false interpretation of prominent pectinate muscles as thrombus and the presence of occult thrombi in multi-lobed appendages is missed.

Doppler Evaluation of Left Atrial Appendage Function

Colour flow imaging guided, Doppler interrogation of left atrial appendage flow should be selected. The sample volume location size is not standardized whether to keep the sample volume at appendage – left atrial junction or at varied sites within the left atrial appendage cavity. The varied location of sample volumes within the appendages will produce significant changes in measured velocities, is also not known. The velocities obtained at the narrowed middle portion of left atrial appendage were higher than the

velocities obtained at the wider orifice of left atrial appendage.

Figure showing Doppler evaluation of LAA by TEE



As a routine colour flow imaging guided, sample volume placement at the site of maximum flow velocities should be employed for left atrial appendage flow. The sample volume placement in the more distal portion of the appendage should be avoided because of Doppler artifacts caused by wall motion. In practice maximal left atrial appendage flow velocities can be

obtained within the proximal third of the appendage.

Doppler Flow Patterns of Appendage in Sinus Rhythm

1) LAA contraction – Positive wave toward the transesophageal transducer. Related to mitral flow in late diastole.[27]
2) LAA filling – Negative wave away from the transducer.
3) Reflection waves during systole – these are passive waves both outward and inward waves that follows contraction and filling waves.
4) Early diastole wave – early emptying wave that correlates with rapid early diastolic inflow into the ventricle.[28]

The early diastolic wave and the appendage contraction wave fuse, resulting in total higher velocities in patients with sinus tachycardia.

Mitral Valve Disease and Left Atrial Appendage

In Mitral stenosis which is hemodynamically significant, there will be increased resistance to left atrial appendage emptying both during active and passive phases. This will cause lowered velocities of left atrial appendage flow, irrespective of the rhythm.

A study by Hwang et al, in patients with rheumatic mitral valve disease and without rheumatic heart disease has also shown that the contraction velocities of left atrial appendage were decreased irrespective of the patients in sinus rhythm and atrial fibrillation. [29]

A study by Lin et al also showed that in patients with atrial fibrillation and mitral stenosis, the normal increase in the left atrial appendage flow during diastole is impaired; this is due to hemodynamically significant stenosis. [30]

In patients with hemodynamically significant mitral stenosis and atrial fibrillation, the velocities obtained from the left atrial appendage will be lower or absent. Whereas in patients with atrial fibrillation and non-rheumatic etiology there is a wide difference in the left atrial appendage flow velocities ranging from ≥ 25cm/ sec which was taken as high and <25 cm/ sec which was taken as low.[31]

The elevated left atrial pressures hemodynamically significant mitral stenosis influences the function of left atrial appendage. Also the inflammatory process off rheumatic heart disease involves the left atrium and left atrial appendage. Another cause is atrial myopathy, resulting from chronically elevated left atrial pressures.

In a study by Lee et al in asymptomatic patients with mitral valve prosthesis, left atrial spontaneous echo contrast was present. This is due to the effect of longstanding pressurised valvular disease on the function of left atrial and left atrial appendage and also due to the stenosis of the prosthetic valve. [32] The recovery of left atrial appendage function following balloon mitral valvotomy is due to the hemodynamic relief of the valvular stenosis. This is due to the fall in the transmitral pressure gradient.

Transesophageal echocardiogram performed after balloon valvotomy showed resumption of left atrial appendage function. This is seen within 24-72 hours post procedure. This effect is also seen in patients with atrial fibrillation as well as in sinus rhythm. [33] Mitral regurgitation on the other hand which is hemodynamically significant also impairs the function of left atrial appendage. This is due to the dilation of left atrial appendage and left atrium and also due to the elevation of filling pressures. In spite of decrease of left atrial appendage function by mitral regurgitation, it also doesn't cause thromboembolism due to the prevention of stasis of blood in left atrium.

There were few studies in the past for patients in sinus rhythm with rheumatic heart disease with mitral valve involvement and its impact on the left atrial appendage dysfunction. Left atrial and left atrial appendage spontaneous echo contrast was more common in patients with reduced flow

velocities of the appendage.

Larger prospective trials should throw light on the possible role of left atrial appendage dysfunction in those patients with sinus rhythm and its implications for future thromboembolic events. This should also address whether left atrial appendage dysfunction also predisposes to the development of atrial fibrillation.

THE MITRAL ANNULUS AND THE MITRAL VALVE

The role of mitral annulus for proper functioning of Mitral valve, left atrium and left ventricle cannot be overemphasized. During systole the mitral annular movement will be towards apex and during diastole the annulus moves towards the left atrium. The movement of the mitral annulus will produce a suction effect and it aids filling of left atrium by a suction effect. The annular movement towards atrium during diastole also aids in emptying of left atrium by reduction of left atrial volume. [34]

Normal Long Axis Function

The left ventricle has both longitudinal and circumferential fibers. The majority of fibers of left ventricle are arranged circumferentially. Both fibers contribute to ejection fraction. The longitudinal fibers contract earlier than

circular fibers. The long axis of the ventricle goes from the apex to the base of the heart. The anatomical definition of the apex is precise, whereas the base of the heart is conveniently fixed at the atrioventricular rings. [35]

The atrio-ventricular interaction is such that during ventricular systole the AV rings moves towards the apex. This leads to the increased volume of atria as its floor move caudally and this creates a suction effect of blood into the atria from pulmonary veins and vena cavae.

The shortening of long axis during systole was around 10-12% and the short axis falls by 25%. This leads to the cavity becoming less spherical. The contribution of longitudinal fibers to the systolic work done by the ventricle is less, in comparison with circumferential fibers. The contribution of longitudinal fibers gain significance due to its important role in mediating AV interactions during systole and diastole.

Zaky and colleagues were the first to describe the mitral annular motion. They initially described the motion of the annulus was from base to apex. Having complex 3D motion pattern, the annular ring as got 3 components

1) Annular motion along long axis of the ventricle from basal region to the apical region.
2) Rotation of the mitral annular ring

3) Sphincter like movements

In a study by Simonson and Pai et al, published in American Journal of Cardiology in the year 1991, showed that a strong correlation exists between left ventricular ejection fraction and the annular displacement during systole measured by M-mode echocardiography. Both longitudinal and radial functions were affected in cardiac diseases. There will be early involvement of long axis myocardial function than the radial function. Tissue Doppler during echocardiographic evaluation helps in the assessment of longitudinal myocardial function. [36]

The calculation of annular velocities is an established method of assessment of global left and right ventricular function. The annular systolic velocity is highest in the lateral annulus. This is due to the abundance of longitudinal fibers in the free wall of left ventricle.

A simple and reliable method for calculating the global and longitudinal left ventricular systolic function is the calculation of mitral annular systolic velocity obtained by tissue Doppler imaging. Lower mitral annular systolic velocity in the septal side is due to the abundance of circular fibers in that area and also due to the influence of right ventricle on the movement of septum.

The pathologic changes that leads to mitral stenosis include

commissural fusion, thickening of mitral apparatus, impaired mobility, calcification and chordal fusion. In a study done by Kuytulos et al published in the Journal of American Society of Echocardiography, showed that reduction in systolic myocardial velocities in mitral stenosis is due to functional changes rather than myocardial pathology. The reduction in myocardial systolic velocities also show a negative correlation with mitral valve area.

METHODOLOGY

STUDY DESIGN

The present study was a prospective study based on semi invasive procedure conducted in the department of cardiology in Madras Medical College and Rajiv Gandhi Government General Hospital for a period of three months from January 2014. Informed written consent was obtained from all the patients prior to the start of the study. Institutional ethics committee approval was obtained.

STUDY POPULATION AND PATIENT SELECTION

The total number of patients selected for the study was 60. The selection criteria of patient were as follows:

INCLUSION CRITERIA

- Patient with moderate to severe Mitral Stenosis with MVO <1.5 cm^2 were included in the study.

EXCLUSION CRITERIA

- Mitral regurgitation – Moderate and severe

- Aortic regurgitation – Moderate and severe
- Aortic stenosis
- Post PTMC or CMC
- Congestive heart failure
- Patients on oral anti-coagulants
- Hypertension
- Hyperthyroidism
- Diabetes mellitus
- Coronary artery disease
- Patient unwilling for transesophageal echocardiography
- Pregnancy and puerperium

METHODS

All eligible patients underwent detailed history and clinical examination. A 12 lead electrocardiogram was taken. Atrial fibrillation diagnosis was based on electrocardiogram.

ECHOCARDIOGRAPHIC DATA

Echocardiographic evaluation was done for all patients with Phillips HD 7XE echocardiographic machine. For transthoracic echo imaging a 2 Megahertz probe and for transesophageal echocardiography 5Megahertz

multi plane probe were used. Various echocardiographic parameters were measured as follows:

1) LVEF

   By modified Simpson's method

2) MVO

   By planimetry in PSAX view

   By Pressure half time

3) Trans-mitral mean gradients

4) Trans-mitral peak gradients

   Calculated using modified Bernoulli equation.

5) LA size (PLAX view)

   AP diameter measured at end systole

6) Tissue Doppler imaging

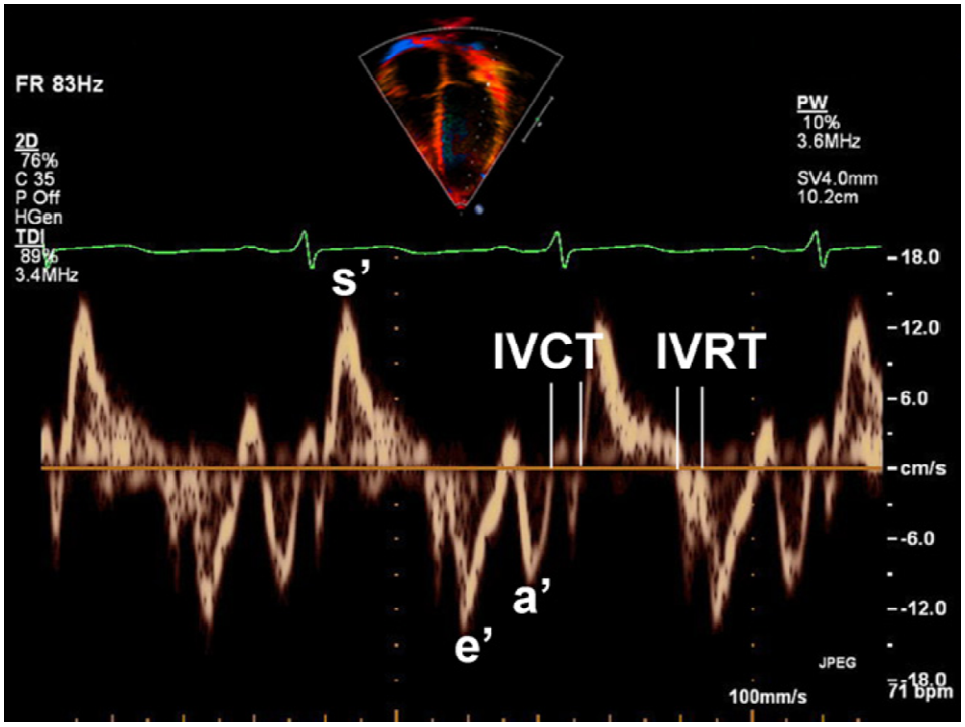
   - A4C view
   - Pulse wave sample volume location – lateral corner of mitral annulus
   - Activation of TDI function
   - Velocity scale selected 30cm/sec
   - Sweep speed selected - 50mm/sec

- Sector angle <60°
- Minimal optimal gain settings such that trans-mitral flow signals eliminated
- Adjustment of Doppler signal filters such that Nquist limit were between -20 and +20 cm/sec

Three important velocities reordered:

1) Systolic myocardial velocity which was a positive wave
2) Em and Am waves which were negative waves and occur during diastole

Figure 1 showing three important velocities in TDI of Mitral annulus



Grading of Mitral Stenosis

Mild 1.5- 2.5 cm^2

Moderate 1.0 – 1.49 cm^2

Severe <1 cm^2

Transesophageal Echocardiography

- Lignocaine was used for local anaesthesia
- LA appendage visualized in 2 orthogonal views
    1) A short axis view in the horizontal plane at the base of the heart at about 45°
    2) With 90° to 120° transducer rotation and counter clockwise rotation of probe

All patients were instructed for fast for at least 4 hours prior to TEE

The thrombus and transduction in left atrial appendage were distinguished by visualizing in more than 1 view. The tuberculation in the appendage were more linear and were in continuity with the atrial wall.

Thrombi tend to project into the left atrial appendage and have an independent motion. Thrombus mobility and size were noted. Size of thrombus was measure in major and minor dimensions.

The appendage was visualized by zooming and the gain settings

optimized to reduce gray-noise artefacts.

Spontaneous ECHO contrast was identified by clouds of echoes which are dynamic and slow curling in a circular shape. The Echo contrast was graded as follows[37]

0 – Absent

1+ - Only mild echogenicity present

Not seen with the gain settings that are used for conventional 2D Echo imaging.

2+ - Mild to moderate echogenicity noted. Seen without optimizing gain settings

3+ - The swirling pattern is moderately dense and was seen throughout the cardiac cycle.

The density is less when compared within the left atrium

4+ - Severe intensity and comparable to those in the main cavity

Pulse Doppler imaging was used to assess the function of left atrial appendage. The sample volume is placed just inside the orifice of the appendage. The maximum velocity during the atrial systole was measured. This velocity was taken as peak LAA emptying velocity. A cutoff value of <25cm/Sec was taken as inactive appendage.

The study population was divided into three groups

Group A1 – Patients in Sinus rhythm and peak emptying velocity of appendage of >25cm/Sec

Group A2 – Patient in Sinus rhythm and peak emptying velocity of appendage of <25cm/Sec

Group B – Patient in Atrial fibrillation

STATISTICAL ANALYSIS

Categorical variables between the groups were compared using chi-square test. Continuous variables are tabulated as Mean and Standard Deviation. Unpaired Student t test had been used for the analysis of the Continuous variables. Then multivariate analysis was done to assess the relative importance to the predictors of the LAA inactivity. The parameters included in multivariate analysis were age, left atrial dimension, mitral valve area, gradients across the mitral valve and S wave velocity. A receiver operator characteristic curve analysis was performed to know the cut-off point of S wave velocity to predict the LA appendage dysfunction in sinus rhythm patients. The statistical analysis was performed by using. Software Package for social Studies (SPSS) Version 17.0.

Figure 2: TEE - Measurement of LA appendage emptying Velocity

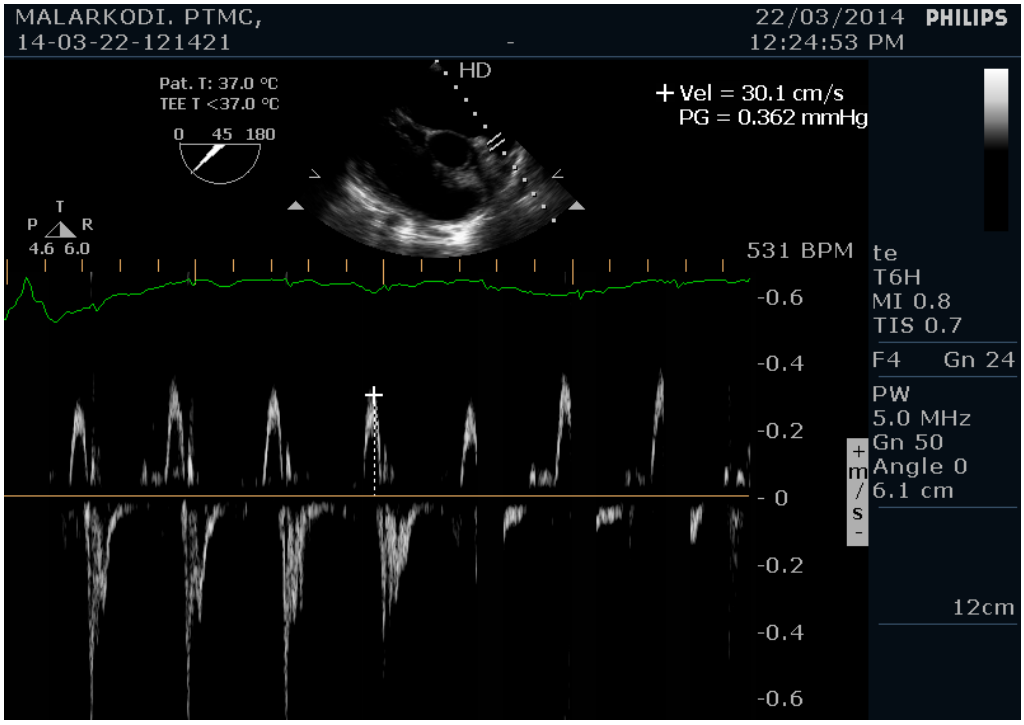


Figure 3: TEE showing LA spontaneous echo contrast

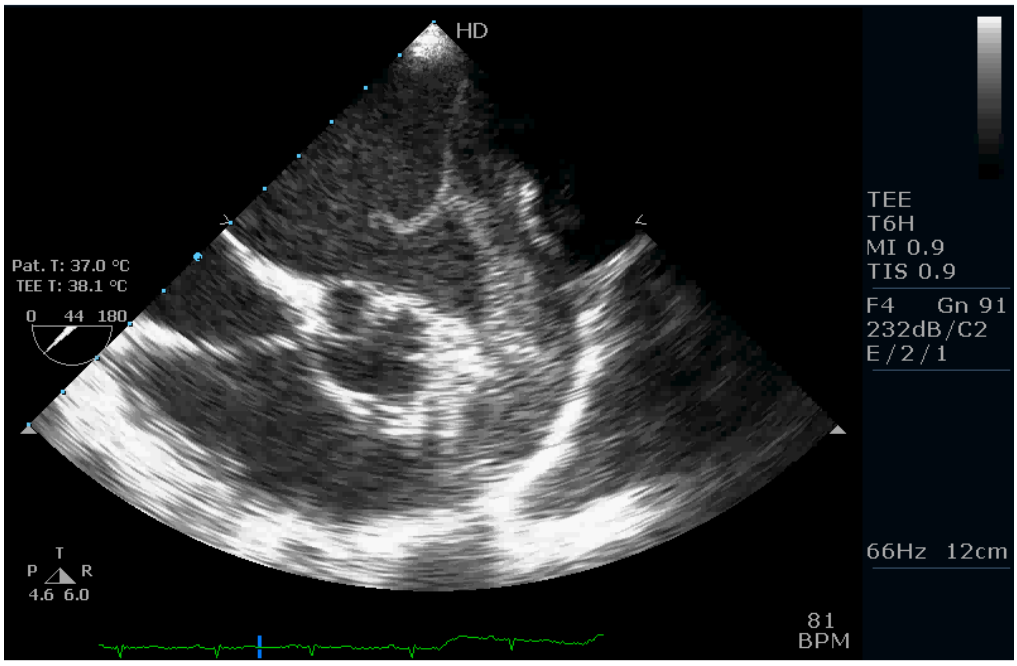


Figure 4: TDI of Lateral Mitral Annulus

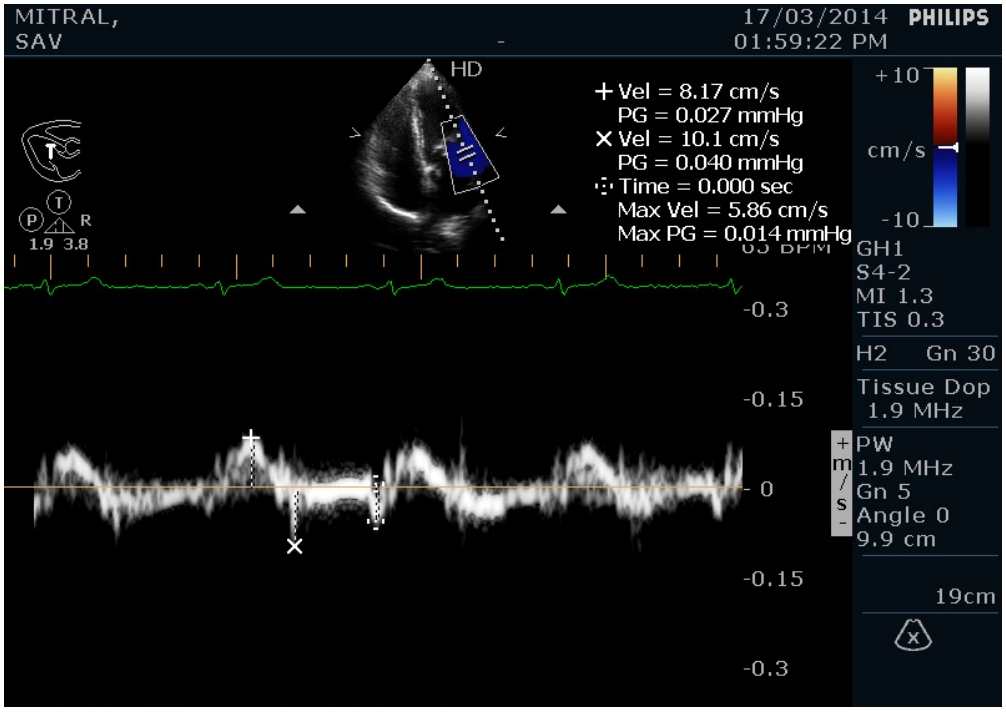
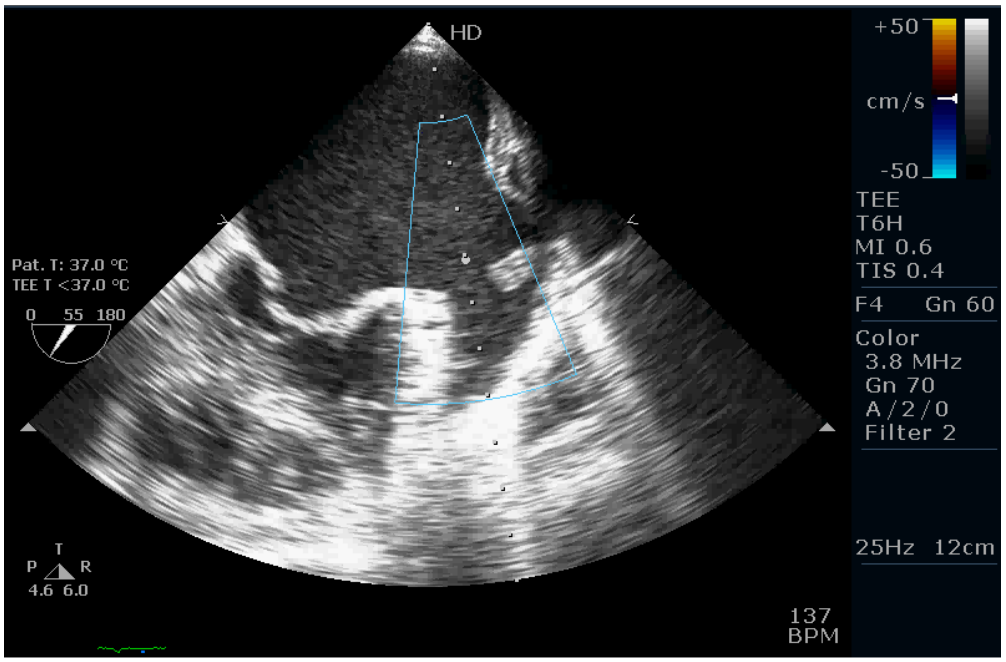


Figure 5: TEE showing LA appendage thrombus



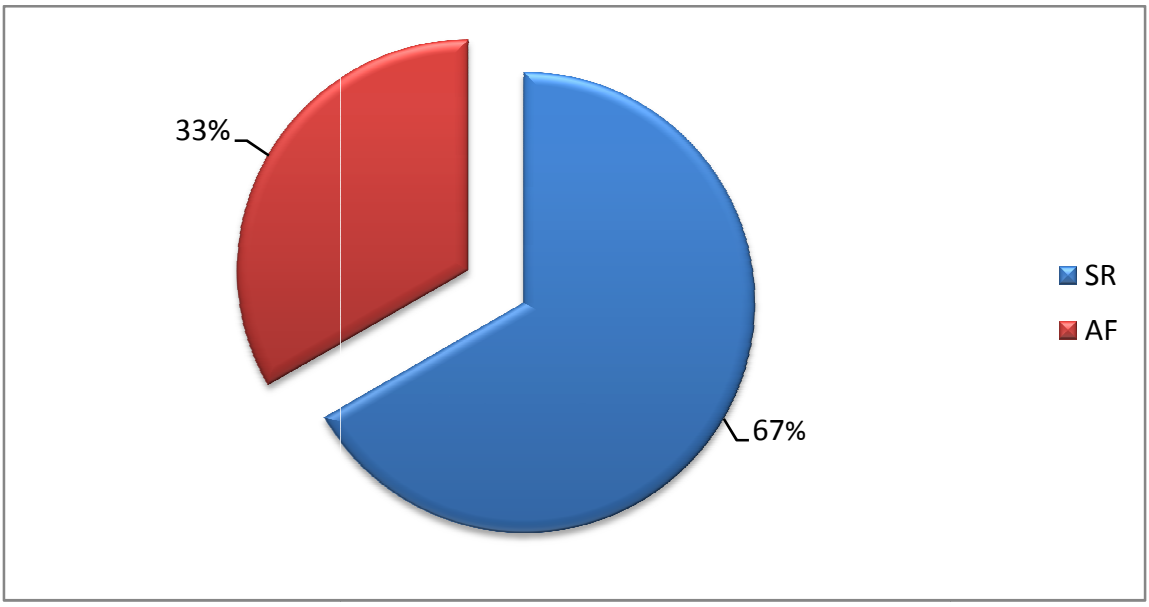
Results and Analysis of Observed Data

Total number of patients in our study were 60. Among 60 patients, 40 were in sinus rhythm constituting 66.7 % of the study population and 20 were in atrial fibrillation constituting 33.3 %. Hence patients were divided into 2 groups, Group A – sinus rhythm patients and Group B – patients with atrial fibrillation. The patient characteristics regarding rhythm is depicted in Table No. 1 and Figure No. 1.

Table No 1: Patient Characteristics

	Patients in Sinus rhythm	Patients in AF	Total
Number of patients	40	20	60
Percentage	66.7 %	33.3 %	100 %

Figure 1: Patient Characteristics

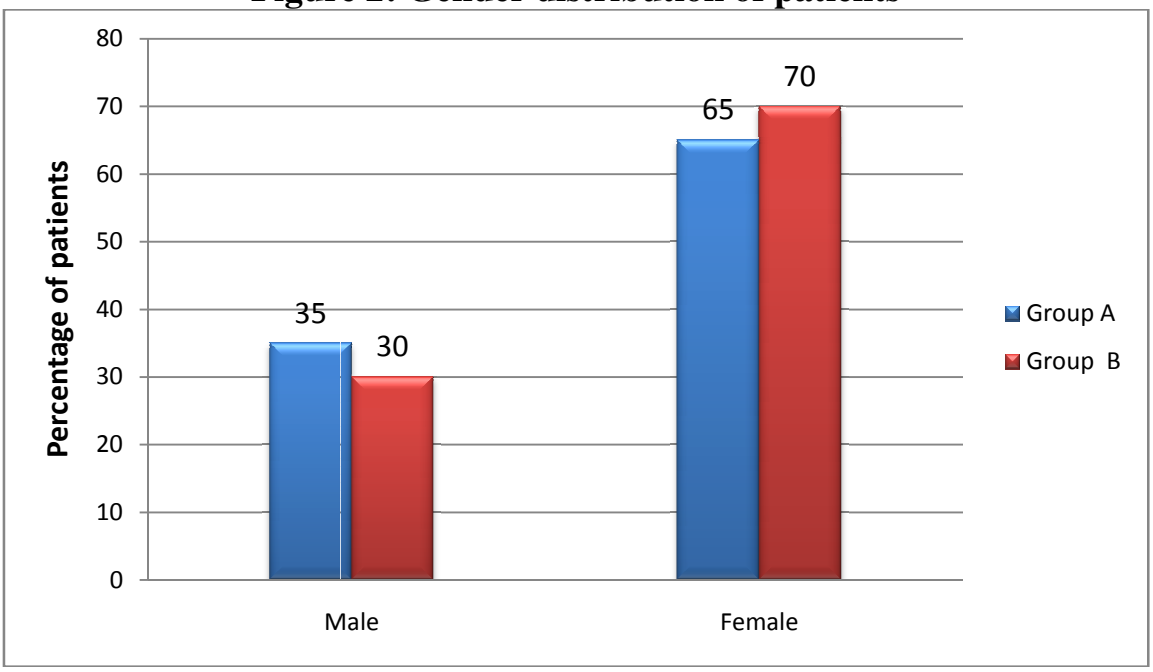


Regarding gender distribution, 20 patients were male among the total study population of 60. Females are more common with 40 patients. Among group A, 14 patients were males and 6 patients were females. In atrial fibrillation group, 14 patients were females and 6 patients were males. In both subgroups female patients outnumbered male patients.

Table 2: Gender distribution of patients

Gender	Group A		Group B	
	No. of patients	Percentage	No. of patients	Percentage
Male	14	35 %	6	30 %
Female	26	65 %	14	70 %
Total	40	100 %	20	100 %

Figure 2: Gender distribution of patients



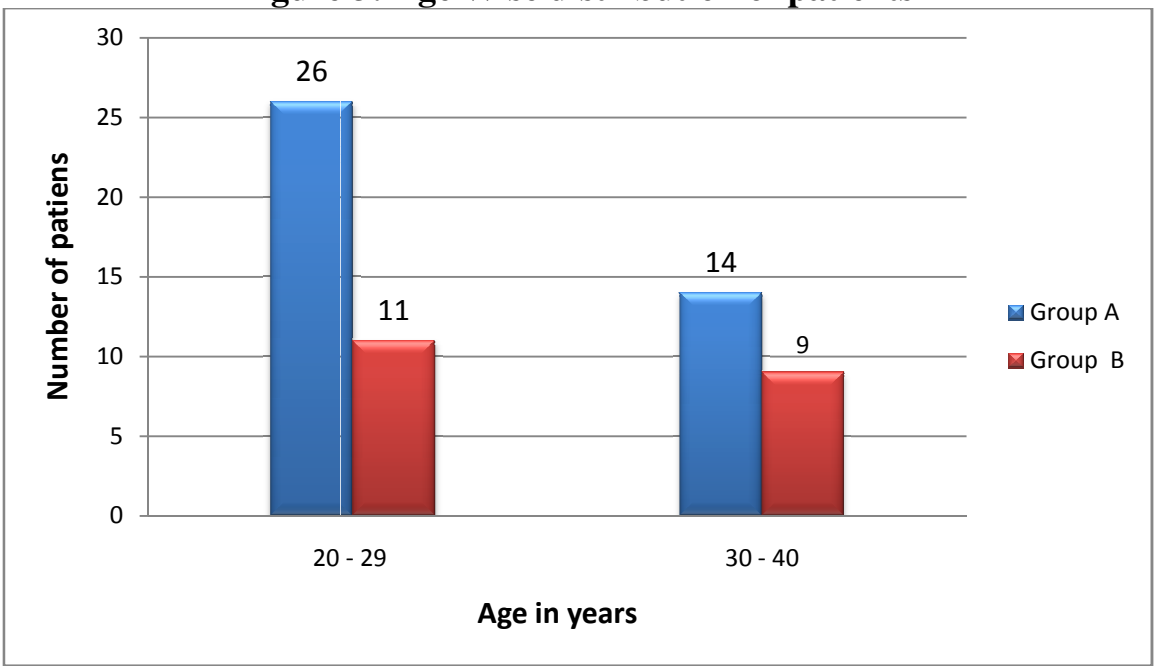
Gender distribution of patients among groups are shown in Table No. 2 and Figure No. 2.

In our study, 37 (61.6 %) patients were in the age group of 20 – 29 years. The remaining 23 patients were in the age group of 30 – 40 years. No patient in our study has age more than 40 years or less than 20 years. In Group A 65 % of the patients were in age group of 20 – 29 years and in Group B 55 % of the patients were in age group of 20- 29 years. The gender and age wise distribution of the study population among groups are not statistically significant. The age wise distribution of the patients are shown in Table no. 3 and in Figure No. 3.

Table 3: Age Wise distribution of patients

Age in years	Group A		Group B	
	No. of patients	Percentage	No. of patients	Percentage
20 - 29	26	65 %	11	55 %
30 - 40	14	35 %	9	45 %
Total	40	100 %	20	100 %

Figure 3: Age Wise distribution of patients



Baseline Characteristics between Group A and Group B

The mean age for Group A is 26.7 years and for Group B is 29.3 which was not statistically significant. The mean left atrial diameter for

Group A patients was 45.7 mm and Group B was 54.5 mm. The difference in LA diameter between the two groups is statistically significant. ($p < 0.001$).

Table 4: Baseline Characteristics

Characteristics	Group A	Group B	p Value	Significance
	Mean ± SD	Mean ± SD		
Age (yrs)	26.73 ± 5.6	29.36 ± 5.7	0.098	NS
Sex (M / F)	14 / 26	6 / 14	0.699	NS
LAD (mm)	45.7 ± 9.1	54.5 ± 7.2	< 0.001	Sig
MVA (cm^2)	1.07 ± 0.18	0.76 ± 0.22	< 0.001	Sig
Ejection Fraction (%)	63.3 ± 2.1	65.1± 1.2	0.087	NS
Mean Gradient (mmHg)	15.0 ± 7.3	11.5 ± 2.5	0.009	Sig
Peak Gradient (mmHg)	22. 5 ± 8.4	21.3 ± 2.7	0.406	NS

Mean mitral valve area is smaller in Group B with mean of 0.76 cm^2 compared to Group A with mean of 1.07 cm^2 . The difference between both groups are statistically significant. ($p < 0.001$). Left ventricular ejection fraction is similar in both groups and does not achieve statistical significance. Mean gradient (MG) across mitral valve was has mean of 15 mmHg in Group A whereas in Group B it is 11.5 mmHg. The difference of means of mean gradient is statistically significant. ($p = 0.009$). The

difference between peak gradients in both the groups was not statistically significant. The mean values and p values are tabulated in Table no. 4

Table 5: TDI and TEE Variables

Characteristics	Group A	Group B	p Value	Significance
	Mean ± SD	Mean ± SD		
Sm Velocity (cm/sec)	17.1± 3.7	12.3 ± 1.0	< 0.0001	Sig
Em (cm/sec)	13.8 ± 1.8	12.7 ± 2.3	0.070	NS
Am (cm/sec)	14.8 ± 2.7	-	-	-
Laaev (cm/sec)	24.3 ± 9.4	4.5 ± 2.2	< 0.001	Sig
% of patients with SEC	22 (55 %)	20 (100%)	< 0.001	Sig
% of patients with thrombus	2 (5%)	11 (55%)	<0.001	Sig

Peak annular systolic velocity (S') is statistically significant between Group A and Group B. ($p<0.0001$). Mean Sm velocity in Group A is 17.1 cm/sec and in Group B is 12. 3 cm/sec. Mean early diastolic annular velocity (Em) is 13.8 cm/sec in Group A and 12.7 cm/sec in Group B. The difference between 2 groups is statistically not significant. Mean late diastolic annular velocity in Group A is 14.8 cm/sec. Group B patients does not have late diastolic velocity as Am wave is absent in atrial fibrillation patients. Left

atrial appendage emptying velocity is different between both groups. In Group A patients the mean Laaev is 24.3 cm/sec and in Group B patients the mean Laaev is 4.5 cm/sec. The difference between both groups is statistically significant. ($p < 0.001$).

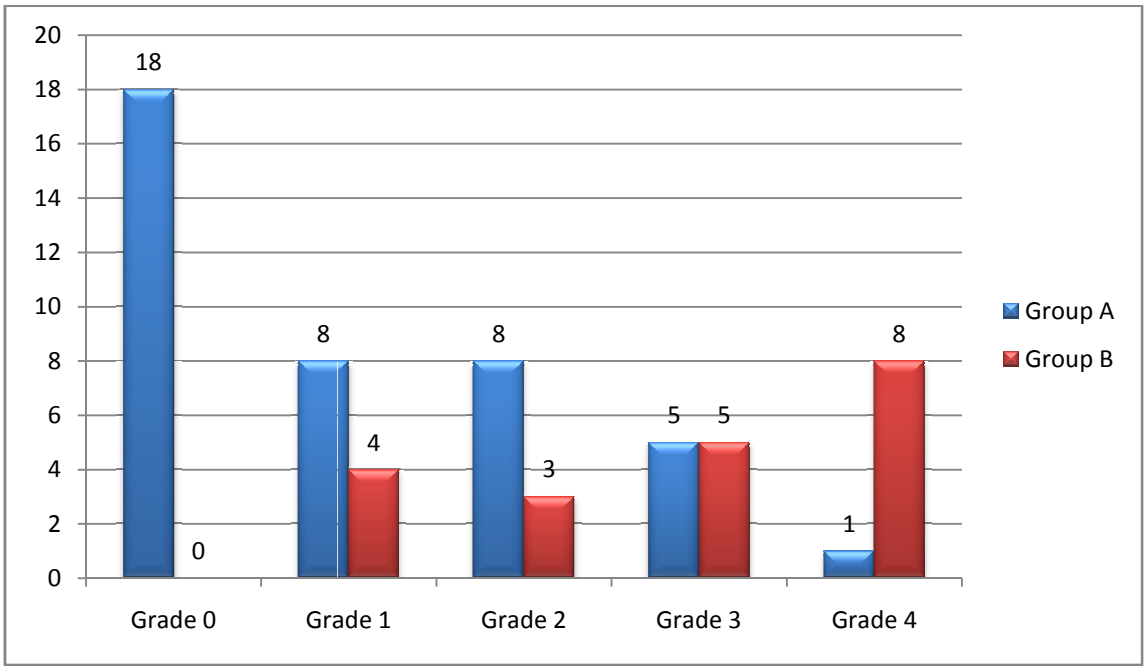
22 patients of Group A were having spontaneous echo contrast (SEC) constituting 55 % of that population. All 20 patients in Group B had spontaneous echo contrast. The difference is statistically significant. ($p < 0.001$). Left atrial appendage thrombus was found in 2 persons in Group A and 11 persons in Group B which corresponds to 5 % and 55 % of the study groups respectively. The difference in occurrence of thrombus is statistically significant. ($p < 0.001$). The details of TDI and TEE findings are tabulated in Table No. 5

18 patients in Group A did not show any spontaneous echo contrast in contrary to Group B patients in whom no one was free of spontaneous echo contrast. In Group B patients, the number of patients is increasing in an ascending pattern as the grade of density of spontaneous echo contrast is increasing. In Group A one patients is having grade 4 SEC whereas in Group B 8 patients are having grade 4 SEC. The differences between both groups regarding the presence of various grades of SEC are statistically significant. ($p < 0.001$). The details are depicted in Table No. 6.

Table 6: Spontaneous Echo contrast density grading

Group	SEC Grading					p Value
	0	**1**	**2**	**3**	**4**	
Group A	18	8	8	5	1	< 0.001
Group B	0	4	3	5	8	
Total	18	12	11	10	9	

Figure 4: Shows trend of SEC density in Groups of patients



Comparison between study groups

The Group A is further sub divided into 2 groups depending upon left

atrial appendage emptying velocity. Group A1 is having left atrial appendage emptying velocity ≥ 25 cm/sec and Group A2 patients were having left atrial emptying velocity < 25 cm/sec. Group B (Atrial Fibrillation group) is kept as such and not subdivided as the Laaev < 25 cm/sec in all cases. The subgroups are compared within for statistical significance as follows.

P1 – Comparison between Group A1 and A2

P2 – Comparison between Group A1 and B

P3 – Comparison between Group A2 and B

The distribution of gender and age groups between all 3 subgroups are not statistically significant when they are compared within them. The mean left atrial dimension was 40.1 mm in Group A1, 50.7 mm in Group A2 and 54.5 mm in Group B. The difference is statistically significant between Group A1 and A2, Groups A1 and B. The difference between Groups A2 and B (P3) is not statistically significant. (p3 = 0.162). There is also a progressive increase in LA dimension when we move from Group A1 to Group A2 to Group B.

Mean mitral valve area is 1.22 cm^2 in Group A1, 0.94 cm^2 in Group A2 and 0.76 cm^2 in Group B. The inter differences in between the three groups is statistically significant. Stenosis severity is progressively increasing from Group A1 to Group A2 to Group B. Left ventricular ejection

fraction does not vary significantly between groups.

Mean gradient and peak gradient were statistically significant between groups. Mean and Peak gradients increase progressively as we move from Group A1 to Group A2. The Peak and mean gradient in Group B is lesser that that of Group A2. The results are tabulated in following Table No. 7

Table 7: Patient Groups Characteristics - TTE

Variable	Group A1	Group A2	Group B	p1	p2	p3
	Mean ± SD	Mean ± SD	Mean ± SD			
Age (Years)	26.74 ± 5.32	27.86 ± 6.3	29.35 ± 5.76	0.539	0.150	0.424
Sex (M / F)	7 / 12	7 / 14	6 / 14	0.816	0.651	0.819
LAD (mm)	40.1 ± 3.2	50.7 ± 9.8	54.5 ± 7.2	< 0.001	< 0.001	0.162
MVA (cm^2)	1.22 ± 0.15	0.94 ± 0.09	0.76 ± 0.20	< 0.001	< 0.001	0.004
EF (%)	63.6 ± 2.5	63.0 ± 1.8	65.1 ± 1.3	0.410	0.082	0.203
MG (mmHg)	8.84 ± 2.1	20.6 ± 5.4	11.5 ± 2.5	< 0.001	< 0.001	< 0.001
PG (mmHg)	15.4 ± 4.0	29.0 ± 5.7	21.3 ± 2.7	< 0.001	< 0.001	< 0.001

Comparing tissue Doppler imaging parameters, the mean peak mitral annular systolic velocity (S wave) is 19.4 cm/sec in Group A1, 15.1 in Group A2 and 12.3 cm/sec in Group B. The differences between these 3 groups are statistically significant. There is progressive decreasing trend in S

wave velocity when we move from Group A1 to Group A2 to Group B. There are no statistically significant variations between early diastolic velocities (Em) of mitral annulus in between sub groups.

As the late diastolic mitral annular velocity (Am) is absent in Groups B (presence of atrial fibrillation abolishes Am wave), it is only compared within Group A1 and A2. The mean Am velocity is 16.1 cm /sec in Group A1 and 13.5 cm/sec in A2. The difference in means and standard deviation between these groups is statistically significant.

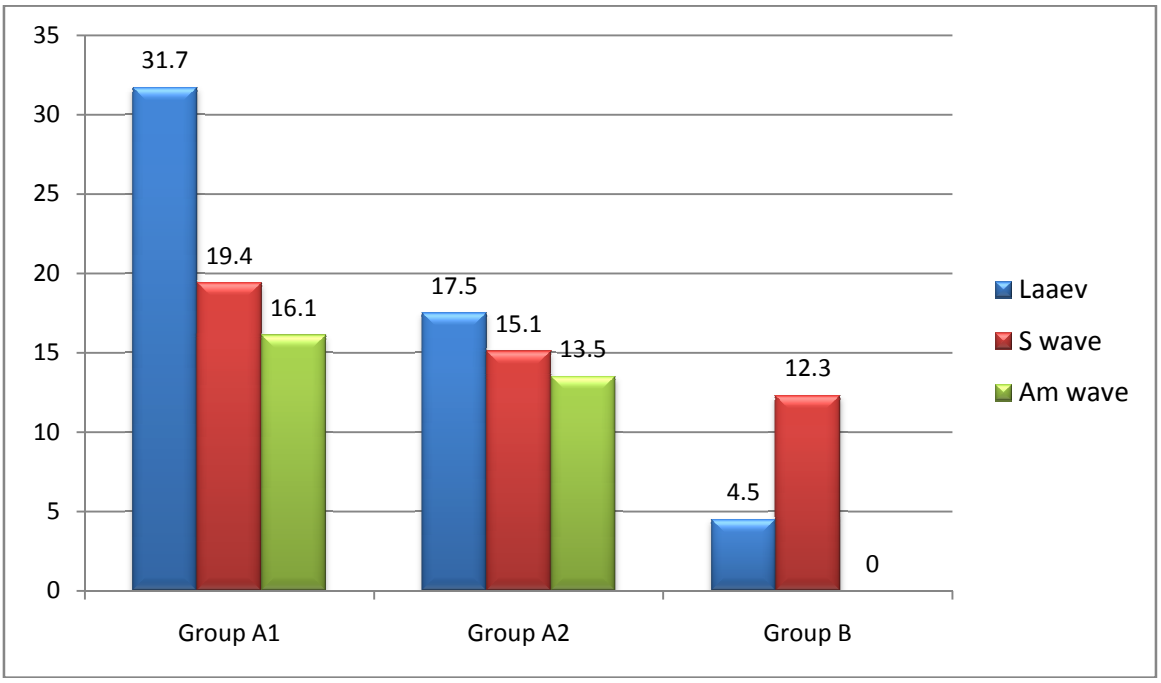
Table 8: Patient Groups Characteristics – TDI & TEE

Variable	Group A1	Group A2	Group B	p1	p2	p3
	Mean ± SD	Mean ± SD	Mean ± SD			
S Wave (cm/s)	19.4 ± 3.5	15.1 ± 2.6	12.3 ± 1.0	< 0.001	< 0.001	< 0.001
Em (cm/s)	14.3 ± 1.7	13.3 ± 1.8	12.7 ± 2.3	0.120	0.072	0.312
Am (cm/s)	16.1 ± 2.2	13.5 ± 2.6	-	0.002	-	-
Laaev (cm/s)	31.7 ± 7.2	17.5 ± 5.2	4.5 ± 2.2	< 0.001	< 0.001	<0.001
% of patients with SEC	3 (15.7 %)	19 (90.4 %)	20 (100 %)	< 0.001	< 0.001	0.157
% of patients with Thrombus	0	2 (9.5 %)	11 (55%)	0.168	< 0.001	0.002

The mean left atrial appendage emptying velocity in Group A1 is 31.7 cm/sec, in Group A2 is 17.5 cm/sec and in Group B is 4.5 cm/sec. There is statistically significant difference between sub groups when analyzed. There

is also a progressive decreasing trend when we move from Group A1 to Group A2 to Group 3. The decreasing trend in Sm wave, Am wave and Laaev is depicted in the figure below.

Figure 5: Bar graph showing decreasing Laaev, Sm and Am wave



3 patients in Group A1 had spontaneous echo contrast constituting 15.7 % pf that population, Group A2 had 19 patients were having SEC constituting 90.4 %. In Group B, all the patients had spontaneous echo contrast. The difference between Groups A1 and A2 and between Group A1 and Group B is statistically significant. The difference between Group A2 and Group B is not statistically significant. ($p = 0.157$). No patients in Group

A1 had any thrombus whereas 2 patients in Group A2 had thrombus. 11 patients in Group B had thrombus as already discussed above. The difference between Group A1 and A2 is statistically not significant (p= 0.168). The difference between Groups A1 & B and Groups A2 & B were statistically significant. The details of differences in TDI and TEE parameters are shown in Table No.8.

16 patients in Group A1 did not show any spontaneous echo contrast, in Group A2 two persons does not have any spontaneous echo contrast in contrary to Group B patients in whom no one was free of spontaneous echo contrast. Grade 3 and Grade 4 SEC is absent in Group A1 patients whereas 5 persons in Group A2 & Group B had Grade 3 spontaneous echo contrast. Grade 4 spontaneous echo contrast is present in only one patient in Group A2 whereas 8 persons in Group B had Grade 4 SEC. The difference is statistically significant as depicted in the Table No. 9 below.

Table 9: Spontaneous Echo contrast density grading within Groups

SEC	Group A1	Group A2	Group B	p1	p2	p3
Grade 0	16	2	0	< 0.001	< 0.001	0.049
Grade 1	2	6	4			
Grade 2	1	7	3			
Grade 3	0	5	5			
Grade 4	0	1	8			
Total	19	21	20			

The relationship between left atrial appendage emptying velocity and peak annular systolic velocity was studied using Pearson correlation. There was positive correlation between these two variables which are statistically significant. (Pearson correlation coefficient r = 0.944, p value < 0.001). The relationship between Laaev and S wave is depicted in scatter plot in Figure No.6.

There was positive correlation between left atrial appendage emptying velocity and mitral annular late diastolic velocity in patients in sinus rhythm. The Pearson Correlation coefficient r = 0.695 (p < 0.001). The relationship is shown in scatter diagram in Figure No. 7

.

Figure 6: Correlation between Laaev and S wave

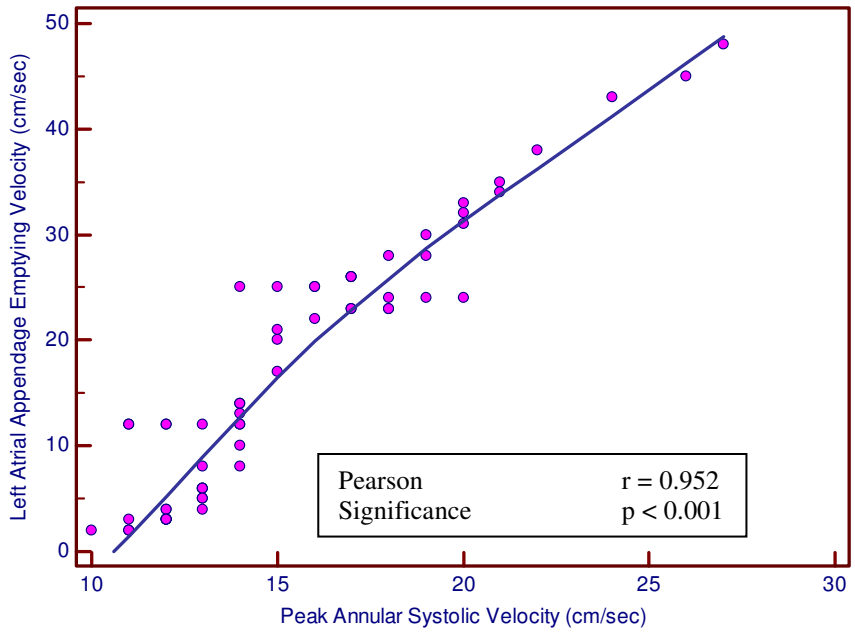
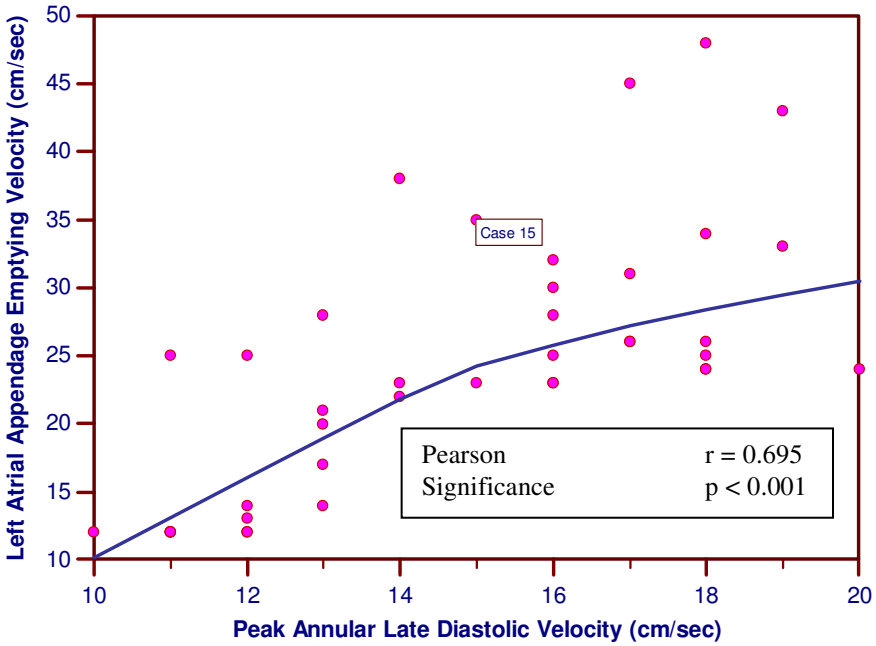
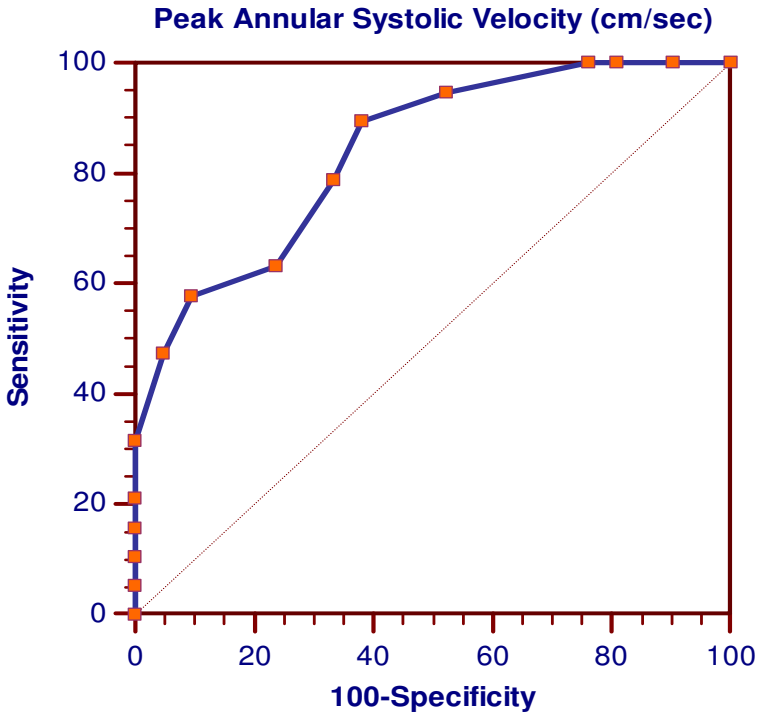


Figure 7: Correlation between Laaev and S wave



The cutoff value of peak annulus systolic velocity which is derived from analysis of receiver operator characteristic curve is 13.5 cm/sec. The area under the curve is 0.840 with confidence interval 0.689 to 0.936 and the p value < 0.001. This value predicts inactive LAA (Laaev < 25 cm/sec) with a sensitivity of 92 % and specificity of 96.5 %. ROC curve is shown in Figure No. 8.

Figure 8: ROC Curve



DISCUSSION

Rheumatic heart disease and the long term consequence of mitral stenosis is a major challenge in many developing countries like India. Over the years a lot of research has been done to understand the pathophysiology and complication of this chronic disorder. Though there has been a good progress, a lot of questions still remain unanswered and contributing to the morbidity associated with this condition.

The major morbidity and mortality in patient with mitral stenosis were due to thromboembolism. Thromboembolic events are more common in patient with mitral stenosis and atrial fibrillation. Patient in sinus rhythm were also at increased risk. Recently much attention has been focused on LA appendage and its emptying velocity.

Anti-coagulants therapy is not introduced for all patients in sinus rhythm. High risk individuals only need anticoagulation treatment. In patients with mitral stenosis the movement of mitral annulus is decreased due to scarring and inflammatory process. In a study done by ozer N et al showed that patients with mitral stenosis long axis function of left ventricle

measured by TDI were reduced. In our study also the annular velocities obtained by tissue Doppler were reduced.[38]

The mean age of patient in our study was 28 years which is in concordance with the world literature. The study population was predominantly female, which is also consistent with epidemiology of the disease. The average age of patients in various studies ranges from 28 – 34 years, with the less predominance of patients over the age 30 years.

In our study positive correlation exists between annular systolic velocity and LAA emptying velocity. In those patients with reduced annular systolic velocities, the left atrial appendage emptying velocity was also reduced. In those patients with reduced annular systolic velocity the spontaneous echo contrast, frequency and density were also increased.

In a study done by Hoiat et al, the left atrial appendage flow velocity was evaluated by altering the loading conditions on the left atrium and they showed that the early emptying velocity was reduced significantly. They also found that the left ventricular systolic function is an important causal factor in the late emptying velocity of the appendage.[8]

In a study published in the Journal of American Society of Echocardiography by Tabata et al, showed that in patients with sinus rhythm

elevated left atrial pressures will decrease left atrial appendage emptying velocity and predisposes to thrombus formation.[39]

In our study patients with left atrial appendage emptying velocity less than 25 cm/s have smaller MVA, higher gradients across the mitral valve and reduction in the annular velocities than patients who have emptying velocities more than 25 cm/s.

In a study done by Sait Mesut et al, they also demonstrated decreased peak mitral annular systolic velocities in patients with mitral stenosis. But they did not compare the annular velocities with emptying velocities. Instead they suggested it could be an early sign of myocardial abnormality.[40]

Previously reported studies showed negative correlation between systolic annular velocity and mitral valve area. But our study showed positive correlation between systolic annular velocity and mitral valve area.

In a study by Bilge et al showed that left atrial emptying velocity was reduced in patients with untreated hypertension. They showed if an elevated after load was imposed on left atrium and appendage, the emptying velocity of the appendage was also reduced. They also demonstrated spontaneous echo contrast and thrombus in those patients.[41]

In a study by Golbasi et al which was done in patients with mitral stenosis and sinus rhythm, left atrial appendage contractile dysfunction is more common in those patients with spontaneous echo contrast.[42]

Our study also showed that group A2 patients with emptying velocity less than 25 cm/s also had increased frequency spontaneous echo contrast and thrombus formation.

Cayli et al also showed in patients with mitral stenosis in sinus rhythm, the presence of spontaneous echo contrast is directly related to the lower annular systolic velocity.[43]

Reported incidence of thrombus in the studies done in the past ranges from 0 to 14% in patients with mitral stenosis and sinus rhythm.

In our study of 21 patients in group A2, two patients had left atrial appendage thrombus. Smaller percentage of thrombus in sinus rhythm patients could be related to our smaller study group.

In our study there was no correlation between Em velocity and left atrial appendage emptying velocity but there is a correlation between Laaev and Am velocity in sinus rhythm patients. Multivariate regression analysis showed that the annular systolic velocity alone is an independent predictor of inactive left atrial appendage. This result showed that long axis function was diminished in mitral stenosis patients and could be the most significant

factor contributing to the appendage dysfunction in mitral stenosis patients with sinus rhythm.

Cut off value obtained by ROC curve for annular systolic velocity is 13.5 cm/sec and this predicts inactive left atrial appendage in mitral stenosis patients.

Atrial Fibrillation Group

These patients had narrower mitral valve area and larger left atrial size as compared to group A patients. Also these patients had lower annular systolic velocities and lower emptying velocities of the left atrial appendage. This finding will explain the increased prevalence of spontaneous echo contrast and thrombus in these group B patients due to significant stasis in the appendage.

In Framingham Heart Study, patients with mitral stenosis and atrial fibrillation have 17 fold increased risk of cerebro-vascular events than control population.[44]

STUDY LIMITATIONS

1. The variables that can be easily accessed by non-invasive echo imaging like mitral valve area, mean and peak gradients and 'S' wave velocity were taken to assess the independent predictors of inactive LAA in patients with sinus rhythm. Other parameter like atrial pressure and stiffness body function were not taken into account.
2. Only patient with isolated mitral stenosis were taken up for the study.
3. Patients with coronary disease and hypertension can have higher cut off value
4. Healthy control population was not compared.
5. Study sample was small. Hence studies with large populations should be done to correlate the above results.

CONCLUSIONS

- In patients with mitral stenosis annular systolic and diastolic velocities acquired by Doppler tissue imaging were reduced.

- Positive correlation is found between mitral annular systolic velocity and left atrial appendage emptying velocity.

- In mitral stenosis patients with sinus rhythm, the systolic annular velocity is an independent predictor of contractile function of LAA.

- In mitral stenosis with sinus rhythm lower annular systolic velocity can be given consideration for anti-coagulation.

- Patients in AF also have reduced mitral annular systolic velocity and LAA contractile function which predicts the higher incidence of SEC and thrombus formation in those patients.

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Master Chart

S. No.	AGE	SEX	AF	LAD	MVA	EF	MG	PG	Sm	Em	Am	LAAEV	SEC Grade	Thrombus
1	24	2	0	38	1.2	63	6	10	26	14	17	45	0	0
2	22	2	0	30	0.9	64	24	31	16	11	14	22	3	0
3	26	1	0	36	1.3	65	7	12	24	14	19	43	0	0
4	32	2	0	43	1.2	63	8	13	18	18	13	28	0	0
5	23	2	1	56	0.6	67	10	16	13	10	0	4	1	0
6	32	1	0	43	0.9	60	25	33	12	11	11	12	1	0
7	28	2	1	42	1.1	63	10	24	11	17	0	2	1	0
8	30	2	0	36	1	64	13	22	19	16	16	30	1	0
9	23	1	0	46	1.3	65	9	15	20	11	19	33	0	0
10	34	2	0	54	0.9	64	25	34	14	14	13	14	3	0
11	22	1	1	55	0.7	66	13	18	13	10	0	8	4	1
12	35	1	1	53	0.7	65	18	20	12	14	0	4	2	0
13	25	2	0	66	0.9	62	25	32	12	16	11	12	2	0
14	21	2	0	36	1	65	27	35	11	12	11	12	1	0
15	23	1	0	39	1.2	62	9	18	16	15	18	25	0	0
16	28	2	1	49	0.6	65	14	24	12	15	0	3	3	1
17	35	2	0	42	1.1	56	9	14	22	14	14	38	0	0
18	20	2	0	46	0.9	64	16	26	17	11	15	23	4	1
19	38	2	0	57	1	63	23	28	15	16	13	17	1	0
20	22	1	1	58	0.8	65	11	21	13	13	0	6	3	0
21	21	1	0	40	1.4	65	9	17	17	16	17	26	0	0
22	30	2	1	62	0.8	66	15	23	13	11	0	6	4	1
23	26	2	0	52	0.7	63	23	28	14	13	12	12	2	0
24	27	2	0	32	1.2	65	8	13	20	13	16	32	0	0
25	23	2	0	40	1.2	64	9	14	27	13	18	48	0	0
26	37	2	0	41	1.3	60	8	13	21	15	15	35	0	0
27	24	1	0	52	1	65	14	24	18	15	16	23	2	0
28	23	2	0	48	1	64	23	29	13	11	11	12	1	0
29	25	2	1	42	0.7	67	12	23	14	12	0	8	3	0
30	38	1	1	56	0.7	66	12	24	12	16	0	3	4	1

Sex : 1 – Male 2- Female Thrombus: 0 – Absent
AF: 0 – SR 1- AF 1 – Present

Master Chart (Contd..)

S. No.	AGE	SEX	AF	LAD	MVA	EF	MG	PG	Sm	Em	Am	LAAEV	SEC Grade	Thrombus
31	20	2	0	38	1.3	62	8	14	15	14	11	25	0	0
32	22	1	0	54	0.9	62	28	42	11	17	10	12	3	1
33	21	1	0	45	1.2	66	9	16	19	13	16	28	0	0
34	32	2	0	40	1	64	12	20	21	14	18	34	1	0
35	23	2	0	41	1.1	66	9	18	16	15	12	25	0	0
36	24	2	0	58	0.8	64	24	27	15	14	13	20	2	0
37	37	1	0	58	1	62	16	27	18	14	16	23	0	0
38	33	2	1	43	0.8	65	11	22	12	11	0	4	4	1
39	32	2	0	48	1.1	64	13	25	14	11	12	12	2	0
40	22	2	0	56	1	62	24	27	14	15	12	13	0	0
41	35	1	1	60	0.6	62	12	18	13	12	0	5	4	1
42	20	2	0	42	1.5	65	6	12	17	16	17	26	0	0
43	29	2	0	40	1.4	62	9	16	20	11	17	31	0	0
44	33	2	0	58	0.9	60	16	27	18	14	18	24	1	0
45	27	1	0	56	1	59	14	25	19	14	18	24	1	0
46	33	1	0	43	1.3	67	6	11	14	14	16	25	0	0
47	29	1	0	41	0.9	65	14	26	17	16	18	26	2	0
48	23	2	1	48	1.4	64	10	18	12	10	0	3	1	0
49	21	2	1	59	0.6	65	14	22	10	15	0	2	3	1
50	35	1	1	53	1.2	65	8	17	13	16	0	6	1	0
51	26	2	0	55	0.9	65	27	42	14	14	12	14	3	0
52	36	2	1	57	0.6	64	13	24	13	15	0	5	4	1
53	36	1	0	48	1.1	62	12	22	15	11	13	21	2	0
54	24	1	0	62	0.9	65	23	21	17	13	14	23	2	0
55	32	2	1	57	0.6	65	8	25	11	11	0	2	4	1
56	39	2	1	57	0.8	66	11	21	14	11	0	10	4	1
57	37	2	0	28	0.9	65	12	24	20	14	20	24	3	0
58	25	2	1	52	0.8	64	9	21	12	10	0	3	2	0
59	28	2	1	72	0.5	65	8	22	11	11	0	3	2	0
60	29	2	1	60	0.7	67	12	24	12	14	0	3	3	1

Sex : 1 – Male 2- Female Thrombus: 0 – Absent
AF: 0 – SR 1- AF 1 – Present

PROFORMA

CORRELATION BETWEEN MITRAL ANNULAR SYSTOLIC VELOCITY AND LEFT ATRIAL APPENDAGE FUNCTION IN MITRAL STENOSIS

NAME: AGE: SEX:
ADDRESS: CD NO:

ECG

ECHO

TRANS THORACIC ECHOCARDIOGRAM

SL. NO.			
01.	LV EF	LV EDV ml	
		LV ESV ml	
		LV EF (MODIFIED SIMPSON)	
		LVIDD cm	
		LVIDS cm	
		EF%	
02.	LA DIMENSION	AP DIAMETER	
03.	MV ORIFICE AREA	PLANIMETRY cm^2	
		PHT cm^2	
04.	MV GRADIENT	PG mmHg	
		MG mmHg	
05.	MVA TDI	S cm/s	
		e' cm/s	
		a' cm/s	

TRANS OESOPHAGEAL ECHOCARDIOGRAM

SL. NO.			
01.	LA APPENDAGE	LATE EMPTYING VELOCITY cm/s	
02.	LAA THROMBUS	SITE	
		SIZE	
		MOBILITY	
03.	SEC GRADING	0	
		1+	
		2+	
		3+	
		4+	

ஆராய்ச்சி தகவல் தாள்

சென்னை அரசு பொது மருத்துவமனையில் **மிட்ரல் வளயிய சிஸ்டாலிக் வேகம் மற்றும் மிட்ரல் இடது ஊற்றறை இணைப்பு வேகம் தொடர்பு மற்றும் மதிப்பாய்வு** இந்த ஆராய்ச்சியில் நீங்கள் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் பங்கேற்பதால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிக்கப்படாது என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியின் முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியில் இருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போதோ அல்லது ஆராய்ச்சியின் முடிவின் போதோ தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கோள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

சுய ஒப்புதல் படிவம்

<u>ஆய்வுசெய்யப்படும்தலைப்பு</u>: மிட்ரல் வளயிய சிஸ்டாலிக் வேகம் மற்றும் மிட்ரல் இடது ஊற்றறை இணைப்பு வேகம் தொடர்பு மற்றும் மதிப்பாய்வு

<u>ஆராய்ச்சி நிலையம்</u>: இருதய மருத்துவத் துறை,
இராஜீவ் காந்தி அரசு பொது மருத்துவமன
மற்றும் சென்னை மருத்துவக்கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர்: **உறவு முறை:**
பங்கு பெறுபவரின் எண்:
பங்கு பெறுபவர் இதனை (√) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களைக் கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது.

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்மந்தமாகவும், மேலும் இது சார்ந்தஆய்வு மேற்கொள்ளும்போதும், இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்துகொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்துகொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறாக நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.

எனக்கு மின் ஒலி இதய வரைவுமார்பகதாண்டு,களத்தாண்டு] பரிசோதனை செய்து கொள்ள சம்மதம்..

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி .....
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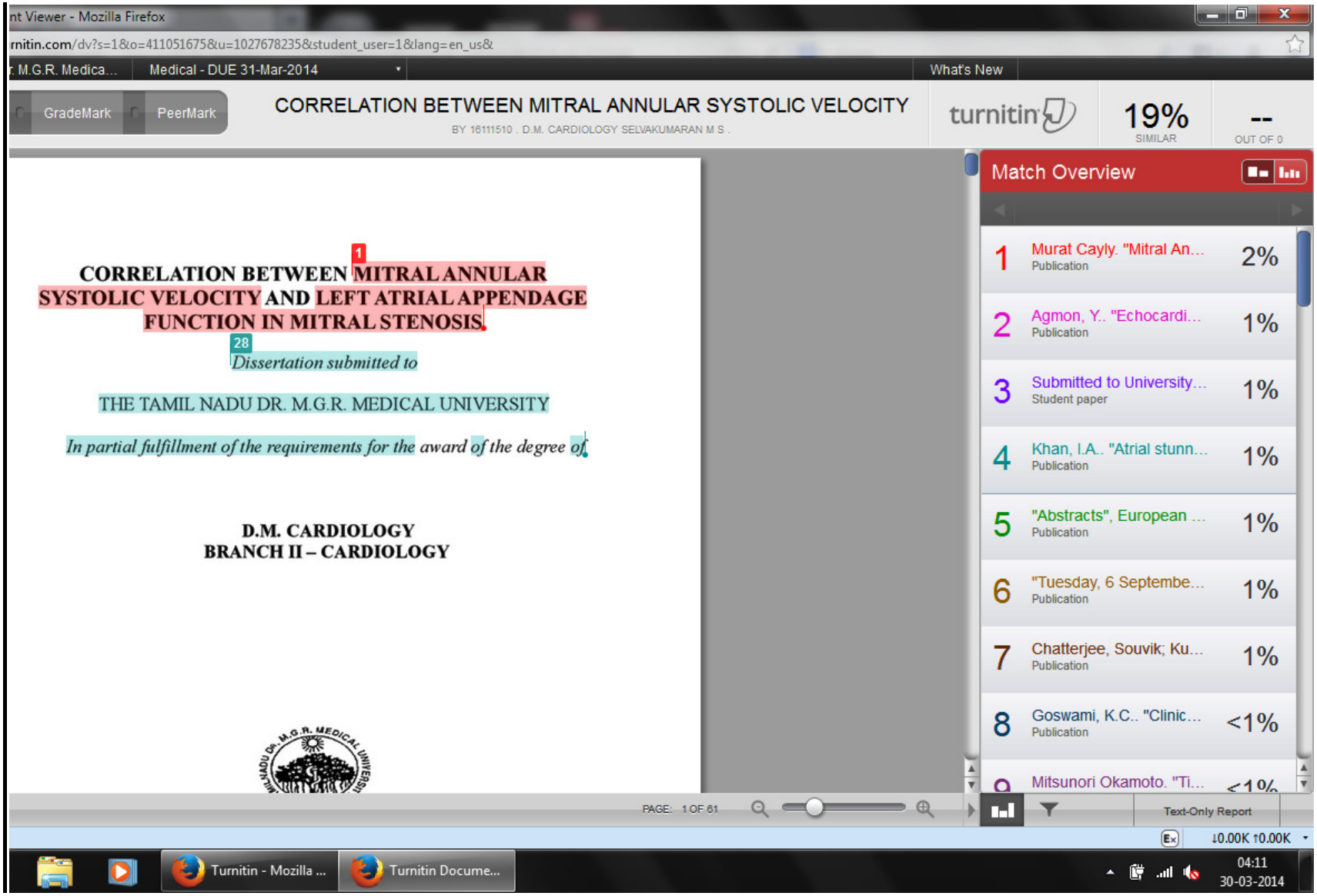
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